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EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/879,792

Applicant(s)

XIAO ET AL.

Examin r

Delia M. Ramirez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-73 is/are pending in the application.
- 4a) Of the above claim(s) 16-21,25,26,28-61,65-68,72 and 73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15,22-24,27,62-64 and 69-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 June 2001 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6, 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 1-73 are pending.

Applicant's election without traverse of Group I, claims 1-15, 22-24, 27, 62-64, 69-71 drawn to DNA, vectors, host cells encoding and expression of the polynucleotide of SEQ ID NO: 11, in Paper No. 8, filed on 8/1/2002 is acknowledged.

Claims 16-21, 25-26, 28-61, 65-68, 72-73 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

1. The specification is objected to for the following reasons: an ATCC deposit is mentioned throughout the specification but no specific deposit number has been indicated. Correction is required.

Priority

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/211224 filed on 6/13/2000, 60/283353 filed on 4/13/2001 and 60/283648 filed on 4/16/2001.

Drawings

3. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review. Applicant is required to submit the

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drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application. In addition, if amendments to the specification are needed due to drawing corrections, Applicant is requested to submit such amendments while the case is being prosecuted to expedite the processing of the application.

Claim Objections

4. Claim 69 is objected to because of the following informalities: a comma instead of a semicolon should be placed in between the terms “polynucleotide specified in (a)-(d)” and “(e) a polynucleotide having...”. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-15, 22-24, 27, 62-64, 69-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1, 6, 11, 22, 27, 62, 69 (claims 2-5, 7-10, 12-15, 23-24, 63-64, 70-71 dependent thereon) are indefinite in the recitation of “ATCC accession No. _____” since the claims are directed to an specific ATCC deposit but no deposit number has been indicated in the claims. Correction is required.

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8. Claims 1, 6, 11, 22, 27, 62 (claims 2-5, 7-10, 12-15, 23-24, 63-64 dependent thereon) are indefinite in the recitation of “biologically active variants thereof” because it renders the claims vague and confusing. While the specification has disclosed the meaning of “biologically active” as it relates to a transmembrane serine protease (page 10, lines 17-19), neither the claims nor the specification have defined this term as it relates to the polypeptide of SEQ ID NO: 12 as recited in the claim and no standard has been provided for ascertaining the requisite degree, therefore one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term “biologically active” can have many different interpretations to one of skill in the art. For example, one interpretation of the term “biologically active” in regard to polypeptides is the ability to elicit antibodies. It is suggested that the term “biologically active” be replaced with a term that clearly defines Applicant’s intended biological function. For examination purposes, the term will be interpreted as “any fragment or variant”. Correction is required.

9. Claim 27 is indefinite in the recitation of “polynucleotide comprising 11 contiguous nucleotides selected from the group consisting of (a) the complement of the nucleotide sequence shown in SEQ ID NO: 11” for the following reasons. First, the term “complement” is indefinite since it is unclear which “complements” are encompassed by the claims. Fragments of any size which are complementary to the polynucleotides claimed can be considered as “complements”. Applicants have not defined the term “complement”, as it relates to size, in the specification either. If applicants wish to claim the entire complementary sequence, it is suggested that the term “complement” be replaced with “complete complement”. Second, as written, the polynucleotide comprises 11 nucleotides wherein the nucleotides are selected from a group but item (a) in the group is a sequence not a nucleotide. Sequences as known in the art are a

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graphical representations of the order at which nucleotides/amino acids are arranged whereas polynucleotides are chemical structures. It is suggested that (a) be amended to recite “the complete complement of the polynucleotide of SEQ ID NO: 11” or similar. For examination purposes, the term will be interpreted as “the complete complement of the polynucleotide of SEQ ID NO: 11”. Correction is required.

10. Claim 27 is indefinite in the recitation of “polynucleotide comprising 11 contiguous nucleotides selected from the group consisting of.....(b) the complement of the coding sequence of the cDNA insert to nucleic acid material of a biological sample to form a hybridization complex” for the following reasons. First, as explained above, the term “complement” is indefinite since it is unclear which “complements” are encompassed by the claims. Second, the claim is directed to a polynucleotide comprising 11 nucleotides wherein the nucleotides are selected from a group but item (b) in the group refers to a coding sequence and not a nucleotide. Third, it is unclear what the meaning of the term “to nucleic acid material of a biological sample to form a hybridization complex” within the context of the claim. For examination purposes, the language recited in (b) will be interpreted as “the complete complement of the cDNA insert of plasmid pCRII-TMSP3”. Correction is required.

11. Claims 27 and 69 (claims 70-71 dependent thereon) are indefinite in the recitation of “polynucleotide that hybridizes under stringent conditions” as it is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. Applicants have disclosed at least two “stringent conditions” in the specification (page 15, lines 3-5). It is suggested that if Applicant’s intended conditions are highly stringent,

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the claims be amended to include the experimental conditions disclosed by Applicants in page 15, since these are recognized as highly stringent conditions in the art (wash conditions 0.2xSSC, 1% SDS at 65 °C). For examination purposes, the term "stringent conditions" will be interpreted as "any hybridization condition". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1, 6, 11, 22, 27, 62, 69-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 6, 11, 62 are directed to genera of polynucleotides of any function encoding any fragment or variant of the polypeptide of SEQ ID NO: 12 or the polypeptide encoded by the plasmid pCRII-TMSP3, vectors or host cells comprising said genera. Claim 22 is directed to a method of producing a polypeptide of any function encoded by the genera of polynucleotides described above. Claim 27 is directed to genera of polynucleotides of any function comprising 11 contiguous nucleotides of (1) the complete complement of the polynucleotide of SEQ ID NO: 11, (2) polynucleotides which hybridize to the polynucleotide of SEQ ID NO: 11, or (3) polynucleotides which encode any fragment or variant of (1) or (2). Claim 69 is directed to genera of polynucleotides of any function which hybridize to the polynucleotide of SEQ ID NO:

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11 or the cDNA of plasmid pCRII-TMSP3 under any conditions or polynucleotides which are fragments, derivatives or variants of the polynucleotide of SEQ ID NO: 11, cDNA of plasmid pCRII-TMSP3 or polynucleotides which hybridize to the above polynucleotides.

While the specification has disclosed the structure of the polypeptide of SEQ ID NO: 12, its corresponding polynucleotide (SEQ ID NO: 11) as well as the function of the polypeptide of SEQ ID NO: 12 (transmembrane serine protease), there is no disclosure of the function of other polynucleotides as encompassed by the claims. No information beyond the disclosure of SEQ ID NO: 11, 12 and its function, has been provided by Applicant which would indicate possession of the claimed genera of polynucleotides. In addition no disclosure of the critical structural elements required for transmembrane serine protease activity, such as the catalytic domain, binding domain, etc. has been provided. No disclosure of which structural elements a polynucleotide which hybridizes to the polynucleotide of SEQ ID NO: 11, a polynucleotide comprising 11 consecutive nucleotides selected from the group as encompassed by the claims, or a polynucleotide encoding a fragment or variant of SEQ ID NO: 12, should have to display serine protease activity.

While one can argue that function can be inferred by sequence comparison with a known protein of known function, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:348-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where

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found to be hydroxylases once tested for activity. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Many functionally unrelated polynucleotides are encompassed within the scope of these claims. The specification only discloses a single species of the claimed genera which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the claimed genera. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

14. Claims 1, 6, 11, 22, 27, 62, 69-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 11, the polynucleotide encoding the polypeptide of SEQ ID NO: 12 or the polynucleotide comprising the cDNA of plasmid pCRII-TMSP3, does not reasonably provide enablement for polynucleotides encoding polypeptides of any function which hybridize under any conditions to the polynucleotide of SEQ ID NO: 11, polynucleotides which comprise fragments or variants of the polynucleotide of SEQ ID NO: 11, polynucleotides which encode fragments or variants of the polypeptide of SEQ ID NO: 12, or polynucleotide which comprise 11 nucleotides selected from the group as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or

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guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The scope of claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides of unknown function encompassed by the claims. While Applicants have disclosed the function and structure of the polypeptide of SEQ ID NO: 12 and the structure of the corresponding polynucleotide (SEQ ID NO: 11), no disclosure of the function of the polynucleotides encompassed by claims has been provided. The specification does not provide any information as to which structural elements are related to transmembrane serine protease activity or the structural elements a polynucleotide as encompassed by the claims should have to display serine protease activity.

As indicated previously, the current state of the art indicates that small amino acid changes can drastically change the function of a polypeptide. See, for example, the teachings of Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998), already discussed. The amino acid sequence of the polypeptide determines its structural and functional properties, therefore, one of skill in the art would require some knowledge and guidance as to how structure is related to function in order to determine the function of a polynucleotide which hybridize under any conditions to the polynucleotide of SEQ ID NO: 11, polynucleotides which comprise fragments or variants of the polynucleotide of SEQ ID NO: 11, polynucleotides which encode fragments or variants of the polypeptide of SEQ ID NO: 12, or polynucleotide which comprise 11 nucleotides selected from the group as encompassed by the claims. Therefore, due to the lack of relevant examples, the amount of

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information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polynucleotides, as encompassed by the claim, with transmembrane serine protease activity. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

15. Claims 62-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition containing an expression vector comprising the polynucleotide set forth in SEQ ID NO:11, the polynucleotide encoding the polypeptide of SEQ ID NO: 12, or the plasmid pCRII-TMSP3, does not reasonably provide enablement for a pharmaceutical composition comprising expression vectors as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

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The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented. The term “pharmaceutical” implies a treatment of a disease. It is unpredictable what diseases can be effectively treated using a “pharmaceutical composition” comprising the claimed expression vectors. Neither the specification nor the prior art provide sufficient guidance as to what specific diseases could be successfully treated by administering a “pharmaceutical composition” comprising the vectors as encompassed by the claim, and attempting to identify a disease treatable using such a “pharmaceutical composition” would constitute undue experimentation. The specification merely provides a large list of diseases from cancer to chronic obstructive pulmonary disease (COPD) in pages 46-52, indicating that cancer and other diseases can be treated with the polynucleotides of the instant invention. There is no indication of therapeutic dosages. Furthermore, even if the specification had provided sufficient guidance as to a disease treatable by administering a “pharmaceutical composition” comprising an expression vector comprising the polynucleotides of the instant invention, the specification provides no guidance as to what, besides the expression vector, would compose such a composition. Making and testing the infinite number of compositions to find one that is effective would constitute undue experimentation. Therefore, the specification fails to enable one of ordinary skill in the art how to make and/or use the “pharmaceutical composition” encompassed by the claim.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 6, 11, 27, and 69-71 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank accession number R78581, June 1995; cited in the IDS). Hillier et al. teaches cDNA encoding a serine protease. The polynucleotide of Hillier et al. comprises a fragment of 151 contiguous nucleotides of SEQ ID NO: 11 (see attached alignment). Hillier et al. also teaches a vector (pT7T3D) comprising said cDNA and a host cell (DH10B) comprising said vector (see Features/source section). Claims 1, 6, 11, 27 and 69-71 are directed to a polynucleotide encoding a fragment or variant of the polypeptide of SEQ ID NO: 12, a polynucleotide which is a fragment or variant of the polynucleotide of SEQ ID NO: 11, vectors comprising said polynucleotides or host cells comprising said vectors. Therefore, the polynucleotide, vector and host cell of Hillier et al. anticipates the claims as written.

17. Claims 1, 6, 11, 27, and 69-71 are rejected under 35 U.S.C. 102(b) as being anticipated by Paolini-Giacobino et al. (Genomics, 44:309-320, 1997; EMBL accession number U75329, Swiss Prot accession number O15393; cited in the IDS). Paolini-Giacobino et al. teaches the cloning of a human transmembrane serine protease. The serine protease of Paolini-Giacobino et al. contains several fragments of the polypeptide of SEQ ID NO: 12 (see attached alignment), therefore the polynucleotide taught by Paolini-Giacobino et al. encodes a polypeptide which is a variant of the polypeptide of SEQ ID NO: 12. The polynucleotide taught by the instant reference is also a polynucleotide which is a derivative of the polynucleotide of SEQ ID NO: 11 since the polynucleotide of SEQ ID NO: 11 can be modified to obtain the polynucleotide of Paolini-Giacobino et al. Paolini-Giacobino et al. also teaches a vector comprising the polynucleotide encoding the serine protease and a host cell comprising said vector. Claims 1, 6, 11, 27 and 69-71 are directed to a polynucleotide encoding a fragment or variant of the

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polypeptide of SEQ ID NO: 12, a polynucleotide which is a fragment or variant of the polynucleotide of SEQ ID NO: 11, vectors comprising said polynucleotides or host cells comprising said vectors. Therefore, the teachings of Paolini-Giacobino et al. anticipate the claims as written.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al. (GenBank accession number R78581, June 1995; cited in the IDS) or Paolini-Giacobino et al. (Genomics, 44:309-320, 1997; EMBL accession number U75329, Swiss Prot accession number O15393; cited in the IDS). The teachings of Hillier et al. and Paolini-Giacobino et al. have been

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discussed above. Neither Hillier et al. nor Paolini-Giacobino et al. teaches the production of the transmembrane serine proteases.

Claim 22 is directed to a method of producing a variant of the polypeptide of SEQ ID NO: 12 by culturing a host cell comprising an expression vector that encodes the variant and isolating the variant.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to cultivate the host cell comprising the vectors, as taught by Hillier et al. or Paolini-Giacobino et al., for the benefit of producing the transmembrane serine proteases of Hillier et al. or Paolini-Giacobino et al. A person of ordinary skill in the art is motivated to recombinantly produce the serine proteases to obtain large amounts of protein for further characterization. One of ordinary skill in the art has a reasonable expectation of success at producing the serine proteases recombinantly since production of proteins by cultivating host cells transformed with a vector that encodes the protein of interest is well-known and widely used in the art. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Conclusion

21. No claim is in condition for allowance.
22. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

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23. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DR
September 6, 2002

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652


REBECCA E. PROCTOR
PRIMARY EXAMINER
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